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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 02/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/719,619	SALLBERG ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-47,51-55 and 57-88* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-47,51-55 and 57-70, 72-88* is/are rejected.

7)☒ Claim(s) *81-88* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/15/2005*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This is to acknowledge the amendment filed 12/15/2005. Claim 1-33, 48-50, 56 and 71 have been canceled. Claims 44, 55, 70 have been amended. New claims 81-88 have been added. Claims 34-47, 51-55, 57-70, 72-88 are pending.

Election/Restrictions

Applicant's election of invention I read on claims 34-47, 51-55, 57-70, 72-88 in the scope of hepatitis C virus antigen in the reply filed on 12/15/2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicants are reminded to amend the claims to the scope of hepatitis C virus for reflecting the examination on the merits.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. (See line 12 on page 6).

Claim Objections

1. Claims 81-84 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claims 51. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the instant case, the claims 81-84 fail to further limit the claimed subject matters set forth in claim 51, instead, the claimed subject matters in those claims have much more other structural characteristics that are not cited in claim 51.

2. Claims 85-88 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim 66. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the instant case, the claims 85-88 fail to further limit

the claimed subject matters set forth in claim 66. Instead, the claimed subject matters in those claims have much more other structural characteristics that are not cited in claim 66.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 47 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains a new matter, which was not described in the specification and in the parental applications that are claimed as priority documents in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the citation of measuring the reduction of viral load cited in claim 47 is a new matter that applicants do not have possession since application was claimed as a continuation of parental applications 09/929,955 or 10/104,966, which claim benefit of provisional application 60/225,767 and 60/229, 175.

5. Claims 34-45, 47, 51-55, 57-70, 72-88 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains new matters, which were not fully described in the specification and were not disclosed in the parental applications that the current application claims as priority documents in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the specific method steps cited in claims 43, 46, 51 and 66 that read on identifying a subject in need of an enhanced production (claim 34) or an increase of titer of IgG antibodies (claim 51) or an improvement in a T cell response (claim 66) are not described in the specification of current application (except the claims 46, 51 and 66) and in the parental applications that applicants claim as continuations of priority documents as stated above. These affect all claims that depended on claims 34, 51 and 66.

MPEP cited in 201.07 [R-1]: A continuation is a second application for the same invention claimed in a prior nonprovisional application and filed before the original prior application becomes abandoned or patented. The continuation application may be filed under 37 CFR 1.53(b) or 1.53(d). The applicant in the continuation application must include at least one inventor named in the prior nonprovisional application. The disclosure presented in the continuation must be the same as that of the original application; i.e., the continuation should not include anything, which would constitute new matter if inserted in the original application. The continuation application must claim the benefit of the prior nonprovisional application under 35 U.S.C. 120 or 365(c).

6. In the instant case, the specification only describe to administer a composition comprising hepatitis C viral antigen and ribavirin, preferably HCV NS3 and/or NS4 to an animal model, which is able to produced an enhanced humoral as well as CD4+ T cell activation. The specification of current application as well as all claimed priority documents do not have any description how each particular immune response is measured or accessed in a subject prior to be selected for using said composition comprising HCV viral antigen and ribavirin. Therefore, applicants are required to cancel the new matter in order to overcome the rejection.

7. Claims 34-47, 51-54, 57-69, 72-80 are rejected under 35 U.S.C. 112, first paragraph, because the specification, because the specification, while being enabling for inducing an enhanced immune response against a specific antigen comprising using a defined viral polypeptide antigen, does not reasonably provide enablement for producing an enhanced specific immune response against a viral antigen with any antigen encoded by an entire viral particle or even an entire HCV particle. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

8. The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art would render undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors were outlined

in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988) set forth below: 1). The nature of invention: 2). Scope of the claim; 3). Level of skill to perform the invention; 4). State of art; 5). Unpredictability in the field, 6). Number of working examples in the specification; 7). Amount of guidance provided by the specification.

9. In the instant case, the claimed invention is drawn to a method for producing an enhanced a specific humoral and cellular immune responses against a specific viral antigen by using a HCV polypeptide of NS3 in combination of ribavirin. The scope of the claims can be reasonable interpreted as any viral antigen that may possibly read on a whole virus or HCV particle in combination with ribavirin.

10. The specification only teaches that a composition made by mixing the full length of NS3 with 1 mg ribavirin (See disclosure at lines 7-18 on page 65 of specification) that is able to induce an enhanced antibody after the composition is administered into a host. However, the specification does not provide sufficient evidence or adequate guidance to support the broadly claimed invention.

11. State of art teaches that HCV NS3 can be made by injecting a plasmid into a host through muscular injection. State of art also teaches that HCV antigenic protein but not the whole HCV genome is able to induce an immune response after administering into an animal. It is unpredictable whether you inject whole coding sequence of HCV genome into a subject will induce an enhanced immune response or produce a replicating or infectious hepatitis C viral RNA since transfecting a subgenomic HCV into a cell line can produce infectious HCV RNA in vitro as evidenced by Lohman et al. (Science 1999, Vol. 285, pp. 110-113, see abstract) or an acute or persistent infection in vivo as evidenced by Forns et al. (PNAS 2000, Vol. 97, pp. 13318-13323, see abstract).

12. The level of skill in the art to perform the full scope of invention should be at the PhD level or holding an advanced degree in virology and immunology for selecting a suitable 10 amino acids and test each of the selections for the ability of inducing an enhanced immune response.

13. Given the above analysis of the factors, which the courts have determined, are critical in asserting whether a claimed invention is enabled, it must be considered that the skilled artisan

would have to conduct undue and excessive experimentation in order to practice the claimed invention.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

15. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

16. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 34-47, 51-55, 57-70, 72-80 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 36-40, 42-55, 57-65 of copending Application No. 10,817,591. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scopes of the current claims can be broadly explained either as a nucleic acid molecule and an amino acid molecule. If the claims are

interpreted as nucleic acid, the scopes of conflict claims are overlapping, and they are obvious versions and anticipated each from other.

18. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. Claims 34-47, 51-55, 57-70, 72-88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hultgren et al (J. Gene. Virol. 1998, Vol. 79, pp. 2381-2391) and Tam (US Patent NO. 5,767,097A).

21. Claimed invention is drawn to a method for inducing both cellular and humoral immune responses comprising administering a composition comprising a polypeptide of HCV NS3 and ribavirin.

22. Tam R. teaches a method for producing an enhanced immune response, preferentially the Th1 type immune response to a specific antigen by administering a composition comprising a viral component with a non-viral component of rebavirin into patients (Claims 1-9). Tam et al. does not teach to use HCV antigen for the co-administration.

23. Hultgren et al. teach a method for inducing an enhanced TH-1 type cellular immune response, such as Th1 type of cytokine secretion, such as IL2 or INFγ (Fig. 5) for HBV e Antigen and Th-1 type humoral immune response for both HBV e antigen (Fig. 4 and 5) and HCV NS3 (Fig. 4) by administering HBV e antigen, core antigen and HCV NS3 in combination of ribavirin at 0.75-1.5 mg per day in mice (See Methods on pages 2382-2383). Hultgren et al. conclude that the co-administration of ribavirin with HCV antigen produces an enhanced Th-1 type humoral and cellular immune response against said specific hepatitis viral antigen.

24. Therefore, on the basis that HCV non-structural protein NS3 is able to induce predominantly induce TH1 type immune responses as disclosed by Hulgren et al. and ribavirin favors to increase the TH1 type immune response by Tam, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by recited references in order to produce an enhanced Th-1 type cellular and humoral immune response against HCV NS3 antigen, to use HCV NS3 and ribavirin in combination to immunize a subject in need absence unexpected result.

25. Regarding to the limitation for co-administering HCV NS3 and ribavirin at one time or separately, it is only considered as a designed choice since the functions exhibited by the two drugs administrated either separately or simultaneously are same. Unless Applicants provide an evidence indicating that the single administration produces more significant result than that administered separately. Hence, the claimed invention as a whole is prima facie obvious absence unexpected result.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the Hultgren et al (J. Gene. Virol. 1998, Vol. 79, pp. 2381-2391).examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 7:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bao Qun Li

BAOQUN LI, MD
PATENT EXAMINER

02/22/2006